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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,573	03/22/2004	Anat Blumenfeld	13572-105014	2196

65989 7590 04/10/2007

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EXAMINER	
MYERS, CARLA J	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/806,573	BLUMENFELD ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-33* is/are pending in the application.

4a) Of the above claim(s) *18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-33* is/are rejected.

7)☒ Claim(s) *26 and 29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II, claims 20-33 in the reply filed on November 15, 2006 is acknowledged. The traversal is on the ground(s) that there would not be any undue burden to examine the nucleic acids of Group I together with the methods of Group II. This argument has been fully considered but is not persuasive. It is maintained that undue burden would be required to examine the claims of Group II together with the claims of Group I as evidenced by the fact that the claims of Groups I and II have acquired a separate status in the art as recognized by their different classification and as recognized by their divergent subject matter. Further, a search of the subject matter of Group I is not co-extensive with a search of Group II and vice versa. In particular, a search for the methods of detecting a polymorphism (group II) would not result in the identification of all relevant prior art teaching nucleic acids that hybridize in the region between D9S127 to D9S59 or D9S53 to D9S105. Accordingly, undue burden would be required to examine the subject matter of Group II together with the subject matter of Group I.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

2. Claims 26 and 29 are objected to because of the following informalities:

In claim 26, the comma in step "c)" following "and the polymorphism," should be deleted and a period should be inserted.

Claim 29 recites "gene associates with" whereas it appears that the claim should recite "gene associated with."

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 26-28 are indefinite over the recitation of "corresponding polymorphism pattern." Corresponding is not an art recognized term to describe the relationship between two nucleic acid sequences or two polymorphism patterns. It is not clear as to whether a corresponding polymorphism or polymorphism pattern refers to polymorphisms of the same identity and at the same nucleotide location within the genome or to polymorphisms of similar identity or at similar locations within the genome (e.g., polymorphisms linked to another polymorphism or located near the polymorphism). Because the term "corresponding" has not been clearly defined in the specification and because there is no art recognized definition for this term as it relates to nucleic acid sequences, one of skill in the art cannot determine what would constitute a corresponding polymorphism pattern and thereby cannot determine the meets and bounds of the claimed subject matter.

Claim 29 is indefinite over the recitation of "typing the subject to determine the maternal polymorphism and paternal polymorphism" because it is unclear as to what is intended to be meant by determining the maternal and paternal polymorphism in the

subject. It is unclear as to what is intended to be the relationship between the subject and the maternal and paternal polymorphisms and it is unclear as to what is meant by determining a polymorphism. Additionally, the claim is indefinite over the recitation in "(e)" of "the polymorphism" because it is unclear as to whether this refers to the maternal or paternal polymorphism or both, particularly since the location of the maternal and paternal polymorphisms are not defined. It is also unclear as to what is intended to be meant by "linking the distribution of the maternal polymorphism and paternal polymorphism with familial dysautonomia" since the claim does not recite a step of determining a distribution and it is unclear as to where the polymorphisms are being distributed. Also, the claim does not recite how this step of linking the distribution pattern relates to the remainder of the claim because the claim does not set forth how this step is used to detect the polymorphism in the subject.

Claims 30-32 are indefinite and vague over the recitation of "typing blood relatives of a subject for a polymorphism" because the claims do not recite how this step relates to the remainder of the claim. The claims omit the relevant steps of using the information obtained from the typing step to accomplish the objective of detecting the presence of a polymorphism linked to a gene associated with familial dysautonomia.

Claim Rejections - 35 USC § 112 – Written Description

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 20-33 are drawn to a method for detecting the presence of a polymorphism linked to a gene associated with familial dysautonomia (FD) comprising analyzing a region of chromosome 9 for a polymorphism located between D9S59 and D9S127 inclusive wherein the presence of the polymorphism is indicative of carriers of a gene associated with familial dysautonomia. The claims do not define the structure of any polymorphisms located between D9S59 to D9S127 (i.e., exclusive of the D9S59 and D9S127 polymorphisms) in terms of their nucleotide identity or location and do not define the gene associated with familial dysautonomia in terms of a particular chemical structure.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to

disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant application, the specification teaches the polymorphisms D9S53, D9S58, D9S105, D9S309, D9S310, D9S172 and D9S174 which are located within the region between D9S59 and D9S127 (see page 38 and Table 1). The specification (page 28) teaches that the region from D9S59 to D9S127 spans about 19 cM of DNA (i.e., approximately 19 million base pairs). Given the extensive size of this region, a significant number of polymorphisms would be expected to occur within this 19 million base pair region. Accordingly, the disclosure of 7 polymorphisms is not considered to be representative of the broadly claimed genus.

Further, the claims require that the polymorphism is linked to a gene associated with FD, such that detection of the polymorphism is indicative of an individual that is a carrier of a gene associated with FD. However, the specification does not disclose any particular genes that are associated with FD. Rather, the specification teaches only a chromosomal fragment from the region of chromosome 9q31-9q33, and particular polymorphic markers within this region that are genetically linked to the occurrence of

FD (see Tables 2 and 3). There are no teachings in the specification or in the prior art as to the length of the gene, the number of introns and exons present in the gene, the positions of the exons and introns in the gene, the precise location of the gene, the nucleotide sequence of any portion of the gene, the sites of initiation or termination of the gene or the functional activity of any protein encoded by the gene. Also, the specification (page 3) refers to "the gene causing familial dysautonomia" and to the "defective gene." However, since all individuals would be considered to be carriers of the FD gene since the gene is present in all individuals, only the mutated gene would be considered to be associated with causing familial dysautonomia. Thereby, the claims appear to also be inclusive of polymorphisms that are linked to a gene that is causative of familial dysautonomia. However, the specification has also not disclosed any genes that cause FD , such a mutated form of a wildtype FD gene. Accordingly, no wildtype FD genes or defective genes causing FD have been disclosed in terms of their complete structure.

It is then determined whether a representative number of species within the claimed genus have been sufficiently described by other relevant identifying characteristics (e.g. restriction map, biological activity of an encoded protein product, etc.). In the instant case, no such identifying characteristics have been provided for additional polymorphisms or for a wildtype or defective gene associated with familial dysautonomia.

While at the time of filing applicants were in possession of the polymorphisms D9S59, D9S127, D9S53, D9S58, D9S105, D9S309, D9S310, D9S172 and D9S174

wherein the polymorphisms are linked to FD and thereby were in possession of methods for detecting said polymorphisms, the limited information provided in the specification is not deemed sufficient to reasonably convey to one of skill in the art, that at the time of filing, Applicants were in possession of the broadly claimed genus of any polymorphism in the region between D9S59 and D9S127, and particularly any polymorphism linked to a wildtype or defective gene associated with familial dysautonomia. Thus the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for detecting the presence of a polymorphism wherein the polymorphism is selected from the group consisting of D9S59, D9S127, D9S53, D9S58, D9S105, D9S309, D9S310, D9S172 and D9S174 , does not reasonably provide enablement for methods for detecting the presence of any polymorphism located between D9S59 to D9S127 wherein the polymorphism is linked to a gene associated with FD and wherein the presence of the polymorphism is

indicative of carriers of a gene associated with FD. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Breadth of the Claims:

Claims 20-33 are drawn to a method for detecting the presence of a polymorphism linked to a gene associated with familial dysautonomia (FD) comprising analyzing a region of chromosome 9 for a polymorphism located between D9S59 and D9S127 inclusive wherein the presence of the polymorphism is indicative of carriers of a gene associated with familial dysautonomia. The claims do not define the structure of the polymorphisms located between D9S59 to D9S127 in terms of their nucleic acid sequence, location or length and do not define the gene associated with familial dysautonomia in terms of a particular nucleic acid sequence. The region from D9S59 to D9S127 spans over 19 cM of DNA or approximately 19 million base pairs (see page 28). Given the extensive size of this region, the claims encompass detecting a significantly large number of polymorphisms that have not been defined in terms of their

nucleotide identity or specific location within chromosome 9. Further, the claims require that the polymorphism is linked to a gene associated with FD, such that detection of the polymorphism is indicative of an individual that is a carrier of a gene associated with FD. However, the gene is not defined in terms of any particular structural features such as the nucleotide sequence of the gene, the length of the gene, the number of introns and exons present in the gene, the positions of the exons and introns in the gene, the precise location of the gene, the sites of initiation or termination of the gene or the functional activity of any protein encoded by the gene. Also, the claims appear to encompass the detection of polymorphisms linked to a defective/mutated gene that is causative of FD and the detection of polymorphisms that are within the FD gene itself and which are causative of FD.

Additionally, claims 26-28 further require correlating the presence of a polymorphism with the presence or absence of the gene associated with FD.

Nature of the Invention

The claims encompass methods of detecting a polymorphism linked to a gene associated with FD. The invention is in a class of inventions which the CAFC has characterized as 'the unpredictable arts such as chemistry and biology" (Mycolgen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Federal Circuit 2001)).

Teachings in the Specification and State of the Art:

The specification teaches the polymorphisms D9S59, D9S127, D9S53, D9S58, D9S105, D9S309, D9S310, D9S172 and D9S174, which are located within the region

between D9S59 and D9S127 (see page 38 and Table 1). The specification also teaches a linkage analysis between these polymorphisms and FD (see, e.g., page 33). Genotyping was performed for 353 different FD chromosomes from 26 linkage families and 148 families with single affected individuals. In particular, the markers D9S127, D9S58 and D9S59 were found to have significant LOD scores, establishing their association with FD (see Figure 2).

The specification (page 3-4) states that linkage analysis can be used to find the location of a gene causing FD. However, the present specification does not actually identify the specific location of the FD gene. Rather, the specification teaches a region of chromosome 9 that is linked to the occurrence of FD.

The specification (page 6) also states that the inheritance of genetic markers within a family can be used to identify individuals that are carriers of a marker indicative of FD because affected individuals will carry the same form of the marker while all unaffected individuals will carry at least one different form of the marker. However, the present claims are not directed to methods for diagnosing risk of developing FD by performing inheritance studies wherein the transmission of a marker from affected family members is detected. Rather, the claims require the detection of any polymorphism between D9S59 to D9S57 as indicative of a carrier of a gene associated with FD.

The Predictability or Unpredictability of the Art and Degree of Experimentation:

The art of identifying polymorphisms that are linked to a gene associated with a disorder is highly unpredictable in the absence of knowledge of the gene itself. It appears that the claims seek to encompass methods which detect the presence of carriers of a gene that is causative of FD. However, the specification does not teach any gene associated with FD and does not teach any defects in a gene that would be causative of FD. The teachings in the specification of polymorphisms present within 9q31 and the teachings that particular polymorphisms in this region are linked to the FD disease is not equivalent to teaching specific wildtype or defective genes that are linked to FD. Knowledge of the presence of a polymorphism linked to FD does not allow one to predict the structure of a gene associated with FD.

Once a region of the genome is identified as being associated with a disease extensive experimentation remains to determine which, if any, genes within this region are sufficiently linked to a disease. Further, once a gene associated with a disease is identified, significant experimentation is required to identify particular mutations and polymorphisms within the gene that are diagnostic of the disease. In the present situation, the ability to isolate the FD gene is particularly unpredictable because no information concerning the functional or structural characteristics of the gene are disclosed in the specification or in the prior art. For example, there are no teachings in the specification or in the prior art as to the length of the gene, the number of introns and exons present in the gene, the precise location of the gene, the nucleotide sequence of any portion of the gene, the sites of initiation or termination of the gene or the functional activity of any protein encoded by the gene.

Amount of Direction or Guidance Provided by the Specification:

The specification does not provide any specific guidance as to how to identify a specific FD gene that is within the region of D9S59 to D9S127. The specification (page 29) states that "(t)the next step of cloning the gene will involve exon trapping, screening of cDNA libraries, Northern blots or rtPCR of autopsy tissues from affected and unaffected individuals, direct sequencing of exons or testing of exons by SSCP (single strand conformation polymorphism), RNase protection or chemical cleavage, or any other state-of-the art technique." While each of these methods was known in the art at the time the invention was made, the outcome of performing such methods is highly unpredictable. The novelty of the claimed invention is not based on general methods for analyzing a region of chromosome 9 by performing exon trapping, Northern blotting etc. Rather, the novelty of the invention is based on the identity of the particular polymorphisms that are to be detected. Since the polymorphisms are defined as being linked to the FD gene, and their presence is characterized as indicative of a carrier of a gene associated with FD, to practice the claimed invention requires knowledge of a gene associated with the occurrence of FD. However, the specification does not provide sufficient guidance as to how to identify such a gene.

Regarding claims 26-28, the claims require correlating the presence of the polymorphism with the presence or absence of the gene associated with FD. However, again, the specification does not teach or provide sufficient guidance as to how to obtain the gene associated with FD. Additionally, these claims require correlating the presence of a polymorphism with a corresponding polymorphism pattern for family

members showing segregation between a polymorphism and the FD gene. However, the specification does not teach any particular polymorphism patterns that are associated with FD. The specification also does not teach how to correlate a polymorphism with a polymorphism pattern. It is unpredictable as to what would be the identity of a specific polymorphism pattern that would be associated with FD.

Further, regarding claim 29, the claim requires linking the distribution of maternal and paternal polymorphisms with FD. However, the specification does not provide sufficient guidance as to how to perform a general step of determining the distribution of a maternal and paternal polymorphism and linking the occurrence of the polymorphism to FD.

Working Examples:

The specification provides working examples of methods for detecting the polymorphisms D9S59, D9S127, D9S53, D9S58, D9S105, D9S309, D9S310, D9S172 and D9S174. However, because the claims do not define the structure of the polymorphism to be detected, the claims encompass the detection of any polymorphism of any identity within a 19 million base pair region of chromosome 9q31. The claims appear to be inclusive of polymorphisms that are within the FD gene itself and which are causative of FD. However, the specification does not exemplify any polymorphisms within an FD gene or any polymorphisms causative of FD. The specification also does not exemplify any particular genes that are associated with FD

or any polymorphisms that are indicative of a carrier of a defective gene associated with FD.

Conclusions:

Case law has established that '(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that '(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that '(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". In the instant case, the claims do not bear a reasonable correlation to the scope of enablement because the specification does not teach any wildtype or defective / mutated genes associated with FD and does not teach a representative number of polymorphisms within the region of D9S59-D9S127 that are linked to a gene associated with FD and indicative of carriers of a gene associated with FD. Although the level of skill in the art of molecular biology is high, given the lack of disclosure in the specification and in the prior art and the unpredictability of the art, it would require undue experimentation for one of skill in the art to make and use the invention as broadly claimed.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20-33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,998,133. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of '133 are both inclusive of methods for detecting the presence of a polymorphism wherein the polymorphism is between the markers D9S53 and D9S105. It is noted that the makers D9S53 and D9S105 are located within the region of D9S59 to D9S127 and the D9S105 marker is within the region of D9S58 to D9S59, as recited in the present claims.

7. Claims 20-33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 5,387,506.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of '506 are both inclusive of methods for detecting the presence of a polymorphism wherein the polymorphism is between the markers HXB and D9S109. It is noted that the makers HXB and D9S109 are located within the region of D9S58 to D9S59 and D9S59 to D9S127, as recited in the present claims.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 20-25 and 30-33 rejected under 35 U.S.C. 102(a) as being anticipated by Kwiatkowski (Genomics. Feb 1992. 12: 220-240; cited in the IDS).

Kwiatkowski (pages 230 and Table 2) teaches a method comprising analyzing human chromosome 9 of a subject and detecting the presence of a D9S59 polymorphism. The D9S59 polymorphism is located "between D9S59 and D9S127 inclusive." Since the present claims specifically include the detection of the D9S59 polymorphism, it is considered to be an inherent property of the D9S59 polymorphism that this polymorphism is linked to a gene that is associated with familial dysautonomia and that detection of the polymorphism necessarily identifies carriers of a gene associated with familial dysautonomia.

Regarding claims 21-25, 31 and 32, it is a property of the D9S59 polymorphism that this polymorphism is located on the q31 band of the long arm of chromosome 9 and is located about 10 to 20cM around the D9S309 and D9S310 markers.

Regarding claims 30-32, Kwiatkowski (e.g., page 230) teaches detecting the presence of the D9S59 polymorphisms in a subject and in blood relatives of a subject.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Carla Myers

Art Unit 1634

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